$11.19 \times 10^7$ cells/kg and $4.78 \times 10^5$ CD34 cells/kg were identified. These cell doses were typically higher than typically seen with UCB grafts because the patients were small (median weight 9.31kg, range 4.75-11.63). All patients successfully engrafted with donor cells and maintained complete donor chimerism post transplant. The median time to engraftment (ANC > 500/uL) was 17 days (range 14-21). Engraftment of platelets (untransfused count of 50K/uL) occurred in 4/5 patients in a median of 72 days (range 31-94). One patient developed acute GvHD (grade 3) and none of the surviving patients (n = 4) developed chronic graft versus host disease. One patient died of progressive liver failure related to GvHD and severe hepato-toxicity 32 days after transplantation. The remaining patients are surviving event-free for a median follow-up of 4.4 years (range 3.3-4.9 years). **Conclusions:** Banked, unrelated donor UCB is a readily available source of allogeneic stem cells for transplantation of patients with FEL. Patients experience durable engraftment and low probabilities of severe acute and chronic GvHD. Thus far, no patients have recurred. UCB transplantation should be considered for all patients with FEL/HLH who do not have a matched related donor.

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### LATE CEREBRAL GRAFT VERSUS HOST REACTION IN A GIRL BONE MARROW TRANSPLANTED BECAUSE OF HURLER (MPS I) DISEASE

*Kyllerman, M.[1], Himmelman, K.[1], Fasth, A.[2], Nordborg, N.[3], Månsson, M.[4] 1. Dept of Neurology, The Queen Silvia Children's Hospital, Göteborg, Sweden; 2. Dept of Oncology/Immunology, The Queen Silvia Children's Hospital, Göteborg, Sweden; 3. Dept of Pathology, Sahlgrenska University Hospital, Göteborg, Sweden; 4. Dept of Clinical Neuroscience, Section of Experimental Neuroscience, Göteborg University, Göteborg, Sweden*

A today 7-year-old girl with Hurler disease (MPS I) underwent bone marrow transplantation at 13 months of age with her one HLA-B antigen mismatched mother as donor. The procedure was complicated by intracranial hypertension, cerebral hemorrhage and shunt operation for hydrocephalus. Symptoms of mild skin graft-versus-host disease (GVHD) developed one year after transplantation and were reversed by prednisolon and cyclosporin. Increased CSF albumin and pleocytosis normalized concomitantly. Ventricular CSF and CNS debris were analyzed by electron microscopy and showed complex aggregates of thin lamellae and electron dense fragments with a tight lamellar texture. Biochemical analysis proved the debris to contain galactosylceramide and sulfatide. The findings were interpreted to represent stripping and desquamation of central myelin sheaths as a result of subacute GVHD reaction in the central nervous system. Her mental development at time of transplantation was in the low normal range to mild mental retardation, while now at 7 years of age she is in the upper range of severe mental retardation. After reversal of the GVHD at 2½ years of age until follow-up at 7 years of age the clinical condition remained stable with no further deterioration. Peters C et al (Blood 1998;91:2601-8) found that GVHD >II has a significant detrimental effect on neuropsychological outcome. CNS GVHD was never part of the GVHD score, but the result of Peters et al could be interpreted as indirect evidence of the presence of CNS GVHD. Our findings, where we had the opportunity to study ventricular fluid cytology and biochemistry, are further evidence for the presence of CNS GVHD. In this case, however, also other factors beside GVHD might add to the poor neuropsychological outcome such cerebral bleeding and ventricular shunt complications.

# SOLID TUMORS

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### INDIUM-111 LABELLED DONOR LYMPHOCYTE INFUSION VIA HEPATIC ARTERY OR I.V. AGAINST LIVER METASTASES OF RENAL AND COLON CARCINOMA AFTER ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION

*Barkholt, L.[1,2], Danielsson, R.[3], Calissendorff, B.[3], Svensson, L.[4], Malihi, R.[5], Uzunel, M.[2], Remberger, M.[2], Ringden, O.[1,2] 1. Centre for Allogeneic Stem Cell Transplantation; 2. Div. of Laboratory Medicine; 3. Dept. of Radiology; 4. Dept. of Medical Physics; 5. Pharmacy, Huddinge University Hospital, Karolinska Institutet, Stockholm, Sweden*

**Objective:** Antitumor effect occurs after allogeneic SCT in patients with metastatic solid cancer. However, this treatment is not as effective against liver as pulmonary and lymph node metastases. To intensify the effect of donor lymphocyte infusion (DLI) against liver metastases, we hereby describe intra-arterial (i.a.) cell injection via the hepatic artery (HA). **Methods:** To trace the infused cells, 3 patients with colorectal, 3 with renal and 1 with breast carcinoma, in a series of 18 SCT patients, were treated with Indium-111 (In-111) oxinate labelled lymphocytes. Four patients received the DLI via HA. They were compared with 2 patients with other metastasis and a patient without CT proven ones using In-111 DLI I.V. **Results:** Localisation of the i.a. In-111 DLI activity on scintigrams corresponded to sites of liver metastases on CT. In contrast, a homogenous isotope uptake over the lungs, spleen and vertebrae was found after DLI I.V. After i.a. injection, the liver to sternum ratio of radioactivity was initially high, but resembled during the following days that of the other patients with I.V. injection. Cells (CD3+, 19+, and 56+) in biopsies of liver metastases in 2 patients treated with i.a. injection were 80-100% of donor origin. Two of 4 patients treated using the i.a. DLI showed regression or stable size and number of liver metastases for 5 and 24 months, respectively. Both are alive 22 and 36 months after SCT. Two of 3 patients receiving DLI I.V. are doing well with a stable metastatic disease or still without liver metastases for 19 and 24 months after cell infusions (24 and 36 months after SCT), respectively. **Conclusion:** When infused via HA, In-111 labelled lymphocytes home to the liver metastases. The majority of liver metastasis infiltrating cells was of donor origin, which supports our aim to provide the DLI focally to liver metastases.

# STEM CELL BIOLOGY

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### OPTIMIZATION OF EX-VIVO EXPANSION CONDITIONS WITH DIFFERENT GROWTH FACTOR COMBINATIONS AND CONCENTRATIONS MAINTAINING LONG-TERM ENGRAFTING ABILITY OF UMBILICAL CORD BLOOD CD34+ STEM CELLS

*Zhang, J.[1], Brown, R.[2], Heye, M.[1], Welhausen, S.[1], Nett, A.[1], Burke, C.[1], Herzig, R.H.[1] 1. James Graham Brown Cancer Center, University of Louisville, Louisville, KY; 2. Quality Biological, Inc., Gaithersburg, MD*

Expanding umbilical cord blood (UCB) stem cell numbers ex vivo for transplantation in adults applications remains a challenge. An improved understanding of how to optimize the cytokines for expansion is needed. The aim of this study was to compare different concentrations of cytokines in combination to define a cytokine combination able to expand the umbilical stem/progenitor cells, especially the immature CD34+CD38-DR-cell subset, putatively responsible for long-term engraftment in vivo. Isolated CD34+ cells from UCB were cultured in a defined serum-free medium (QBSF-60) with stem cell factor, Flt-3 ligand, thrombopoietin, IL-3, IL-6 IL-11, G-CSF, and erythropoietin. Two different concentrations of cytokines were used; group 1 with a higher concentration, representing a 10-fold (one log) increase over the other, group 2. Fresh media with cytokines was supplemented or exchanged at day 4, 7, and 10. The clonogenic efficiency, $CD34^+$ sub-populations and the expansion potential were determined on day 7 and day 14 by evaluating the following parameters: clonogenic progenitors(CFU-GM, BFU-E, CFU-GEMM and HPP-CFC) and immunophenotypes($CD34^+$ cells and $CD34^+$ sub-populations) The expansion was done over a 14 day culture period. The day 7 fold expansion was similar for both groups 1 and 2 (data not shown). By day 14, group 1 yielded more nucleated cells (with IL-3) of 971 ± 75 fold expansion compared with 305 ± 55 fold expansion in group 2 and CD34+ cells (with IL-3 and IL-6) of 33 ± 4.5 and 26 ± 4.9 fold-expansion compared with 6.8 ± 2.2 and 16 ± 5.9 fold-expansion in group 2. Further, group 1 culture containing IL-6 yielded more CD34+CD38-DR-cells of 31 ± 12 fold-expansion compared with 11 ± 2.1 fold-expansion in group 2. The higher concentration group also produced more CFU-C and